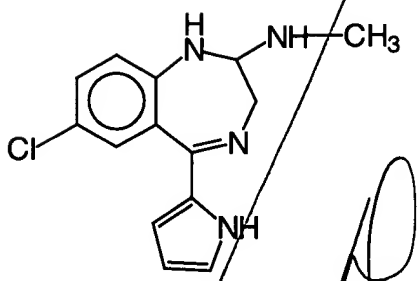


RO-24-7429

REMARKS

The present invention relates to a pharmaceutical composition comprising: (a) a therapeutically effective amount of a tumor necrosis factor inhibitor; (b) a therapeutically effective amount of a compound selected from the group consisting of reverse transcriptase inhibitors, protease inhibitor, a gene inhibitor, myristoylation inhibitors, cell-virus binding inhibitors, LTR promoter site inhibitors, ribosome inactivators, platelet aggregation inhibitors and prophylactic and therapeutic HIV vaccines, and (c) a pharmaceutical inert nontoxic carrier. The compositions of the invention are therapeutic cocktails useful for the treatment of HIV and related syndromes associated with HIV. As applicant will show, therapeutic cocktails are important in the treatment of acquired immunodefficiency syndromes (AIDS).

THE REJECTION UNDER 35 U.S.C. § 103(a)

Claims 1, 2, 4, 12 and 21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the Makonkawkeyoon et al reference taken with the Pardee et al

patent. In view of the claim amendments now directed to an enhanced combination, it is respectfully submitted that this rejection is now moot.

The treatment of HIV requires a multitude of cocktails to attack each biochemical pathway which the virus uses to replicate. Because thalidomide is an immunomodulator, its use in combination with other therapeutic agents will help enhance the modulating action of the other drugs. The AIDS syndrome attacks many organs and accordingly immunomodulation is desirable. The drug RO 24-7429 typically inhibits the tat gene to exert its anti-HIV effect while at the same time thalidomide exerts its effect as an immunomodulator. In anti-HIV therapy, the immunomodulatory effect of thalidomide will exert a beneficial effect by reducing harmful protein factors which are producing runaway inflammatory conditions (attacking a multitude of organs) in patients afflicted with AIDS. The prior art is silent regarding the combination of thalidomide with a gene inhibitor.

The Office has failed to establish the criteria necessary to establish a *prima facie* case of obviousness as set forth in MPEP § 2142: the cited reference must teach or suggest all the claim limitations; there must be some motivation or suggestion, either in the reference or in the knowledge available to the skilled artisan, to modify the reference to arrive at the claimed invention, and there must be a reasonable expectation of success. Applicants vigorously disagree with the assertion in the Office Action stating that one skilled in the art would reasonably expect to arrive at the compositions of the present invention. The Office has failed to show where in *Makonkawkeyoon et al* or *Pardee et al* there is a teaching or suggestion of the use of thalidomide in combination with a protease inhibitor to treat HIV. It is additionally

submitted that *Makonkawkeyoon et al* or *Pardee et al* are each deficient in expressly teaching or suggesting the embodiments of the present invention, as recited in the pending claims.

At most, the cited art might give an inference to try to do what Applicants have done. There is usually an element of "obvious to try" in any research endeavor, since such research is not undertaken with complete blindness but with some semblance of a chance of success. However, "obvious to try" is not a valid test of patentability. *Hybritech Inc. v. Monoclonal Antibodies, Inc. (CAFC 1986) 231 USPQ 81; In re Geiger (CAFC 1987) 2 USPQ2d 1276; In re Dow Chemical (CAFC 1988) 5 USPQ2d 1529.* Patentability determinations based on "obvious to try" are contrary to § 103 of the statute.

The compositions and method of the present invention are not obvious because none of the references alone or in combination disclose or suggest the use of thalidomide in combination with other gene inhibitors for treating HIV.

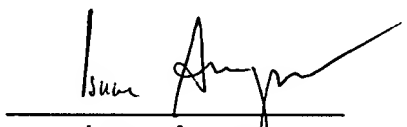
Applicant respectfully submits that the elected combination of thalidomide with the anti-HIV drug RO-24-7429 is patentable. Accordingly, Applicant requests the Examiner to extend consideration on the merits to additional species in accordance with M.P.E.P 809.02(c) (2) (I) and 37 C.F.R. 1.141.

THE REJECTION UNDER 35 U.S.C. § 112

In view of the claim amendments, it is believed that the rejection under 35 U.S.C. § 112, has been rendered moot.

In view of the above remarks, favorable reconsideration and withdrawal of the rejection under 35 USC § 103 is respectfully requested. The Examiner is invited to contact the undersigned at 703-418-2777 if he feels that an interview of the present case would facilitate the resolution of any outstanding issues. An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,



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